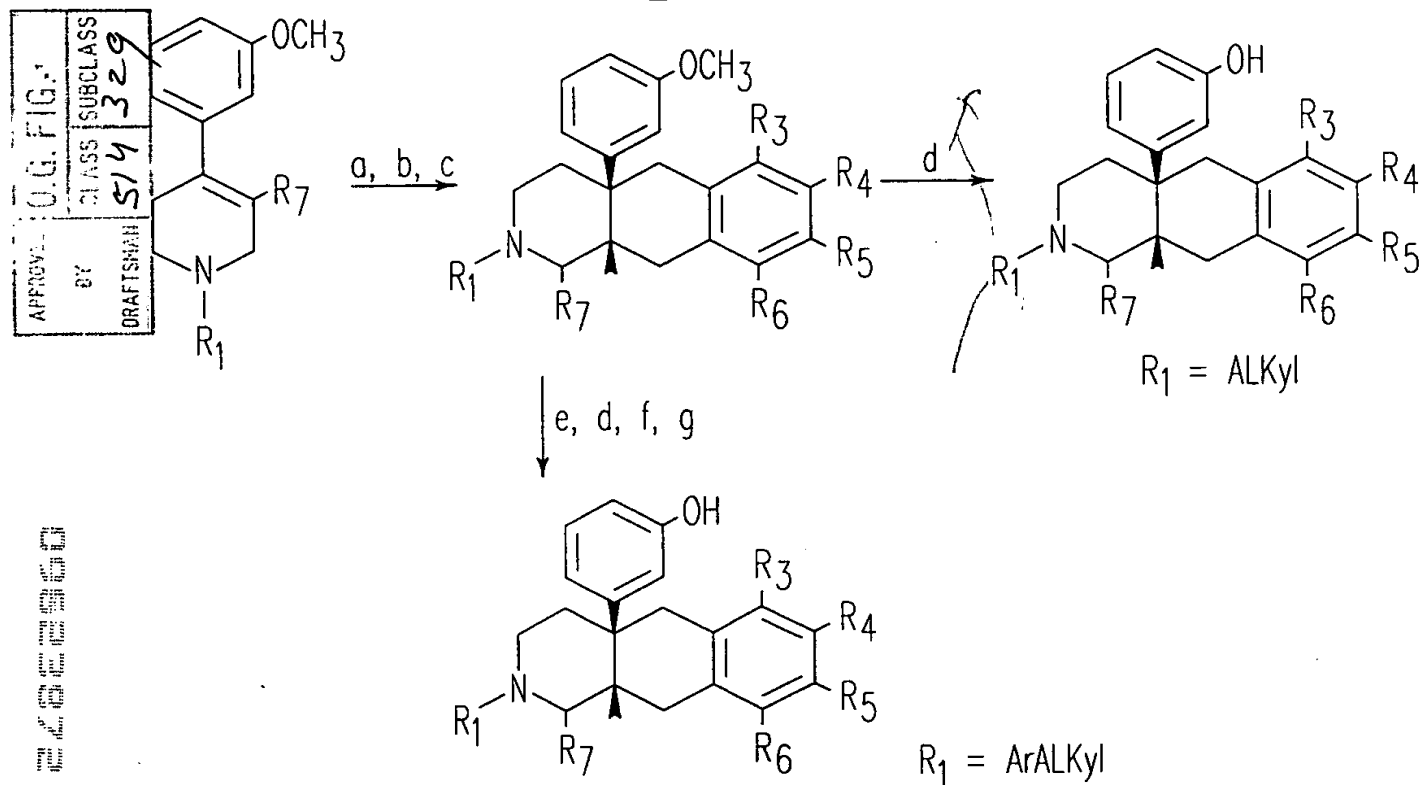


FIG. 1



Reagents: (a) $s\text{-BuLi}$, THF; AND

(b) NaI , CH_3CN ;

(c) NaBH_4 , EtOH ;

(d) HBr , HOAc ;

(e) PhOCOCl , toluene;

(f) aryl-alkyl- COOH , BOP, triethylamine, THF,

(g) borane/THF

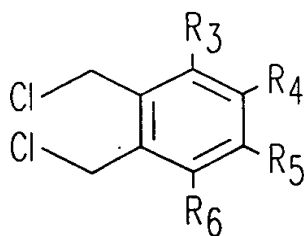
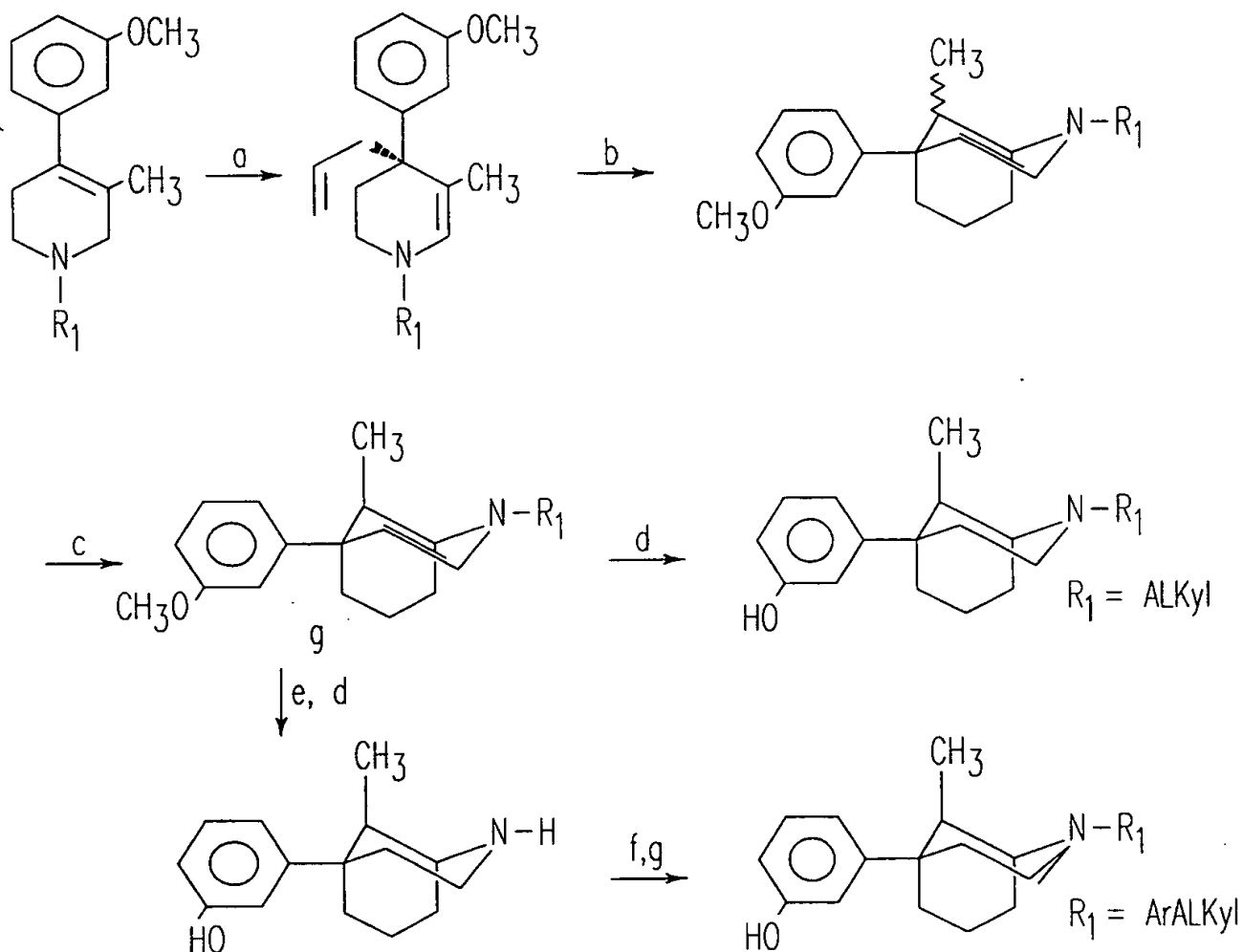
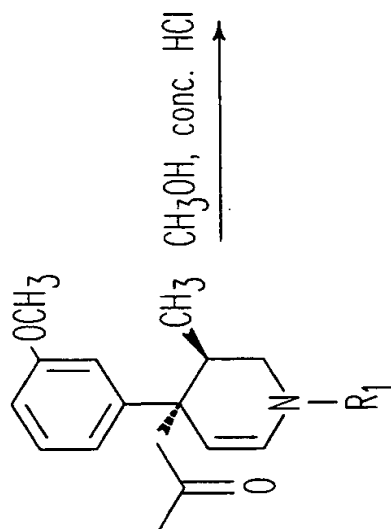
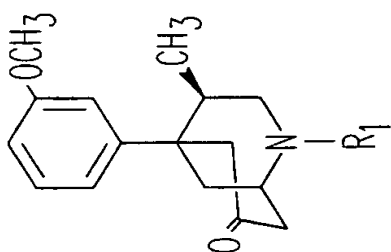


FIG. 2A

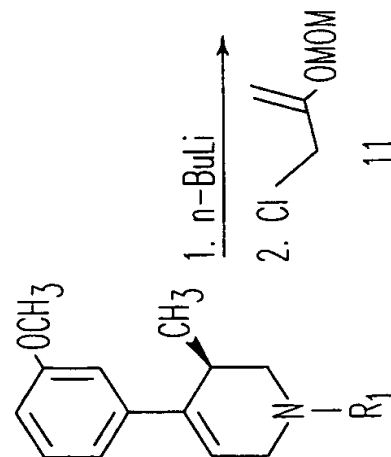


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FIG. 2B



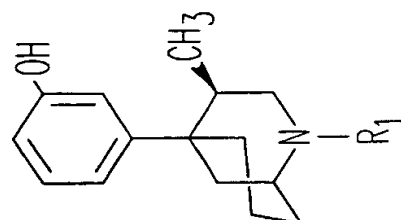
CH₃OH, conc. HCl



1. n-BuLi
2. Cl-CH₂-CH=CH-OMOM

11

3. 2N HCl



1. Zn, HCl
2. HBr, HOAc

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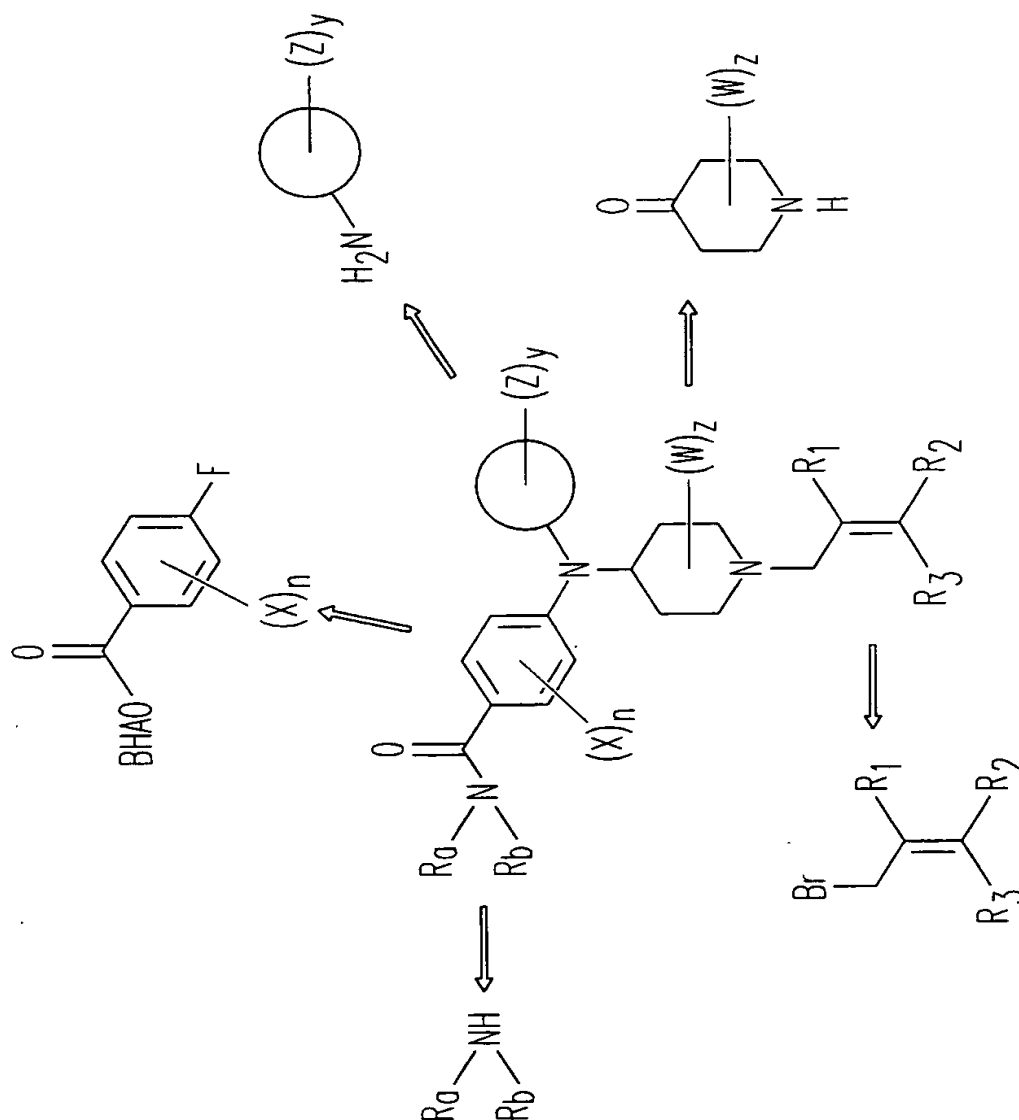
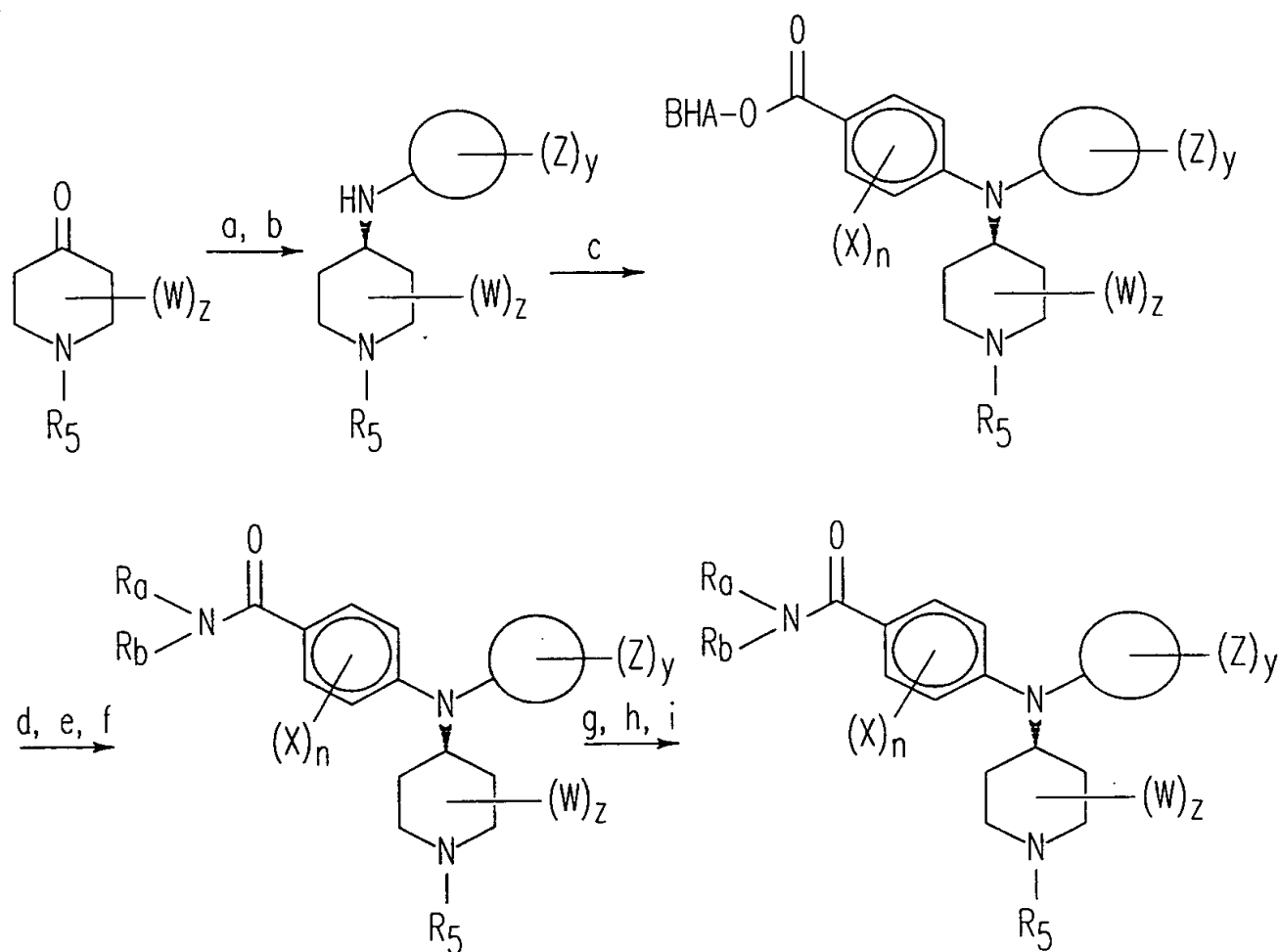
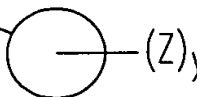


FIG. 3

FIG. 4



Reagents: (A) $Ti(O-i-Pr)_4$, $:NH$  $(Z)_y$

(b) $NaBH_4$, EtOH;

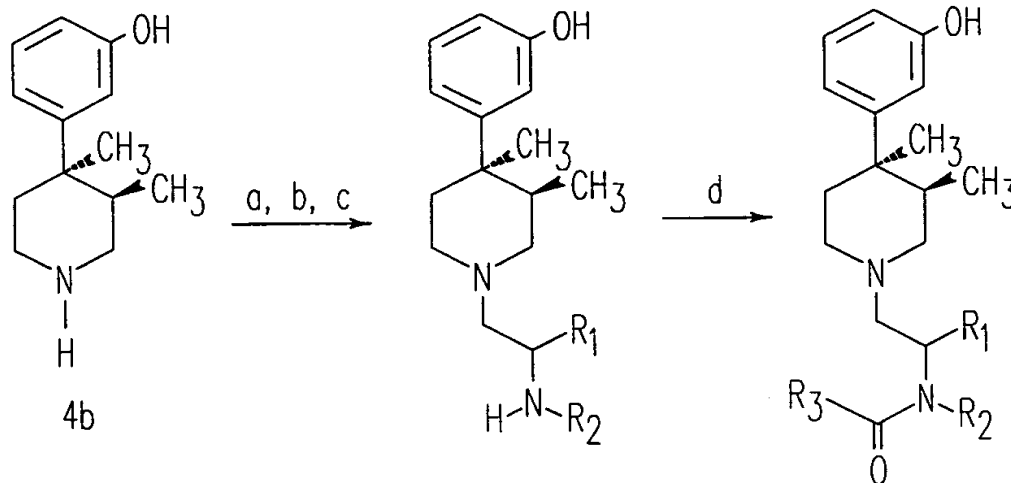
(c) $n-BuLi$, THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzoate;

(d) N-methylpyrrolidinone, $NaOCH_3$, toluene; (e) EtOH, H_2O ;

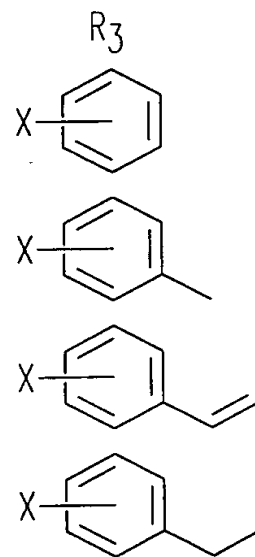
(f) R_aR_bNH , BOP, Et_3N ; (g) $PhOCOCl$;

(h) KOH, $i-PrOH$, H_2O ; (i) R_5-Br , EtOH, K_2CO_3

FIG. 5



	R ₁	R ₂
6a,	H	H
b,	H	CH ₃
c,	CH ₃	H
d,	CH ₃	CH ₃
e,	i-Pr	H
f,	i-Pr	H
g,	i-Bu	H
h,	s-Bu	H
i,	c-Hex	H
j,	Ph	CH ₃
k,	Bn	H



X=OH, OMe, OEt, OBn,
OnBu, OPh, Me, iPr, Bu,
Ph, NMe₂, CONH₂, F, Cl, Br.

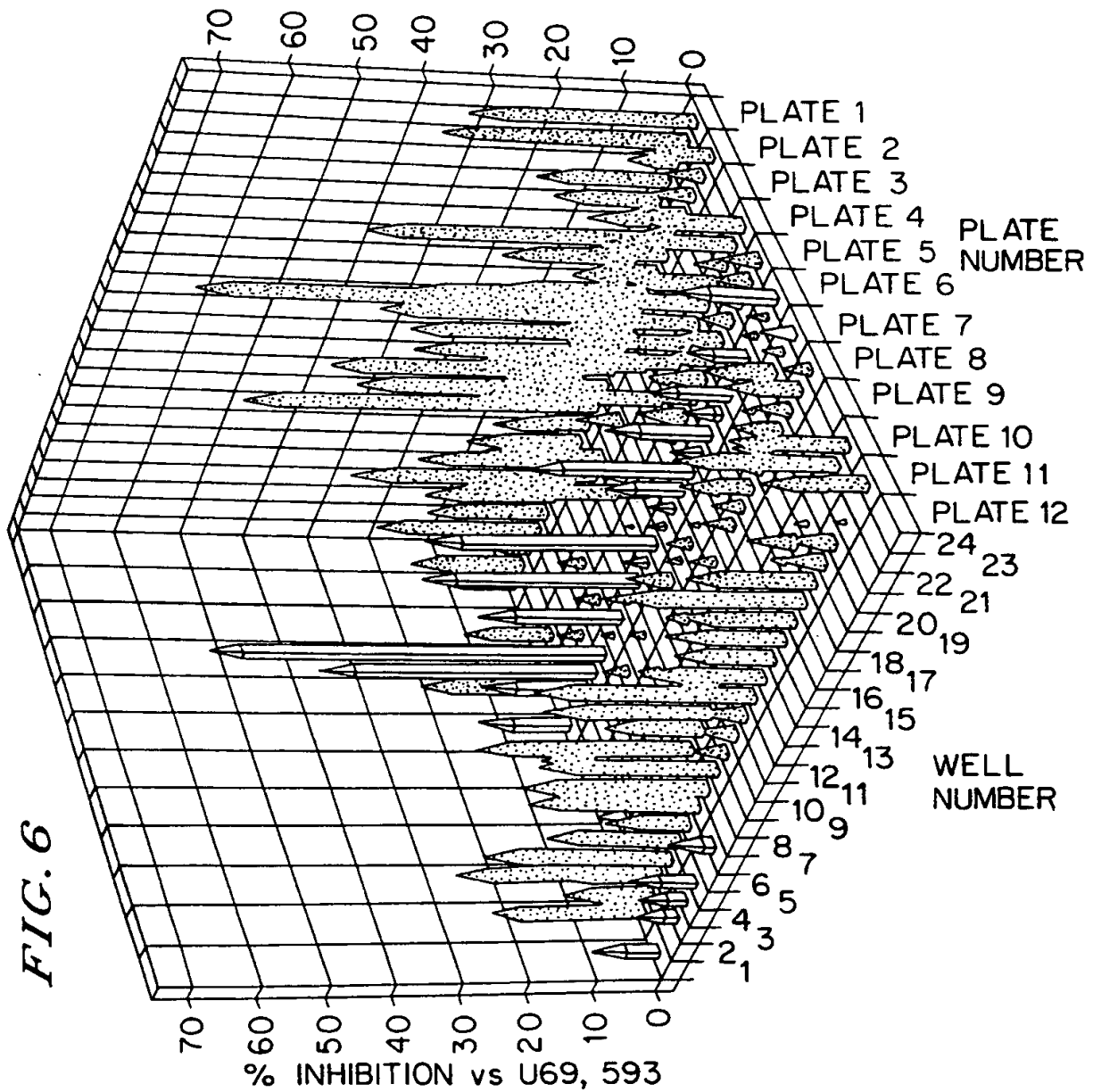
^aReagents: (a) Boc-amino acid, BOP, TEA, THF;

(b) TFA, CH₂Cl₂;

(c) borane/dimethyl sulfide;

(d) R₃CO₂H, BOP, TEA, THF.

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Substitute Sheet (Rule 26)

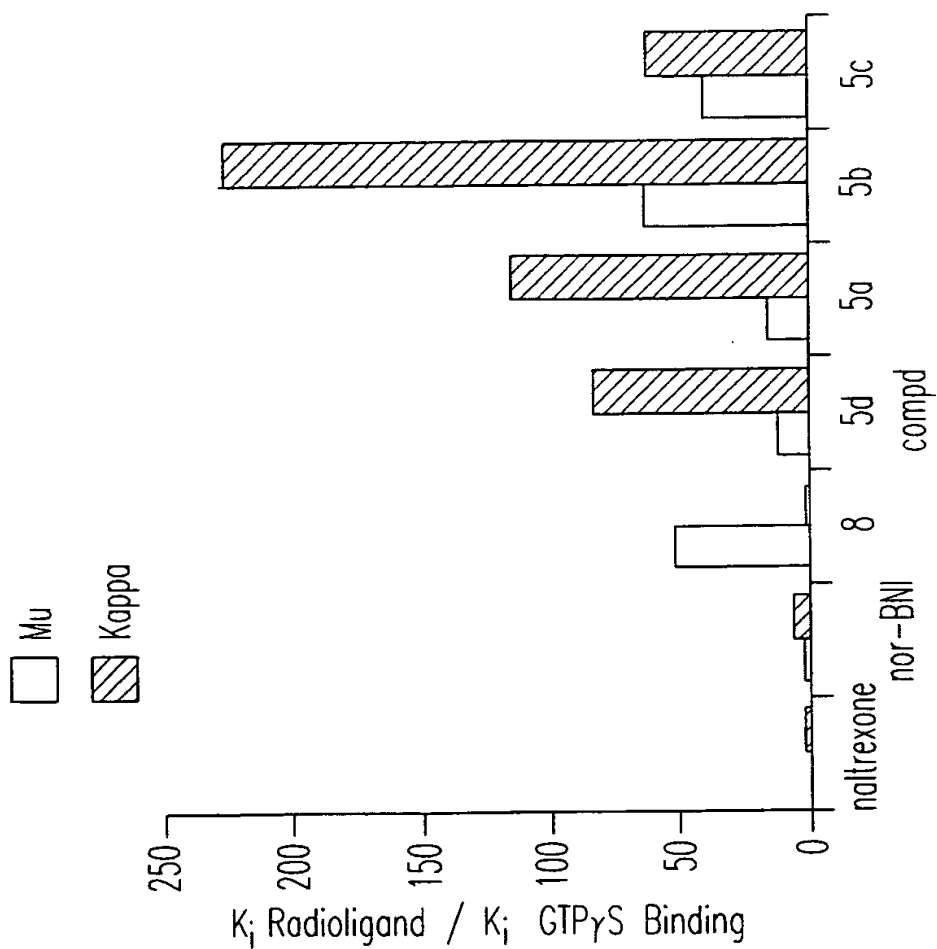
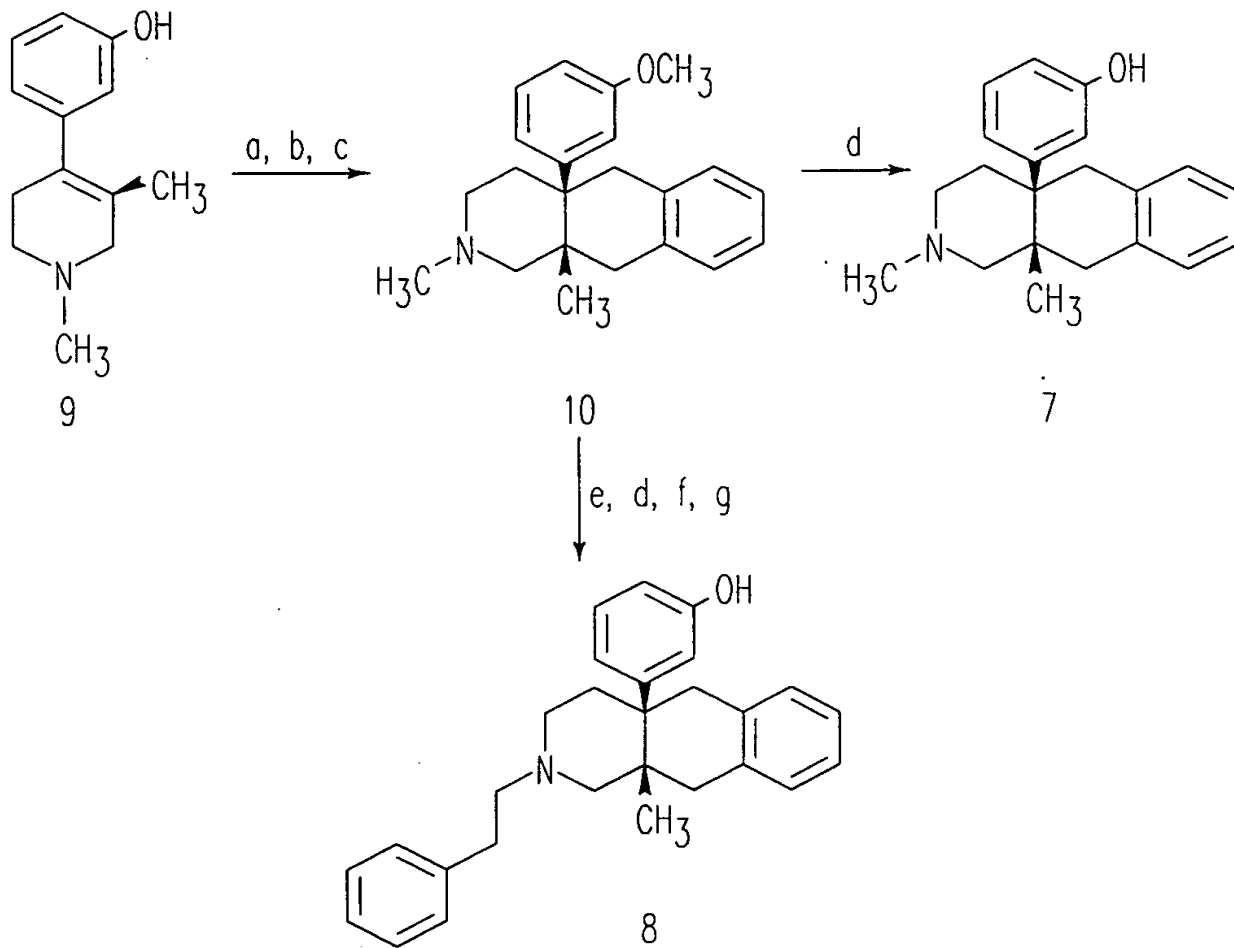


FIG. 7

FIG. 8

(a) $s\text{-BuLi}$, THF; α,α' -dichloroxylene;(e) PhOCOCl , toluene;(b) NaI , CH_3CN ;

(f) Phenyl Acetic Acid, BOP, TEA, THF;

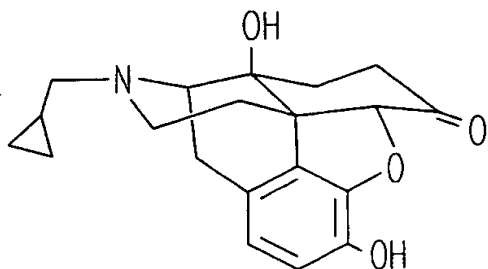
(c) NaBH_4 , EtOH;

(g) Borane/THF;

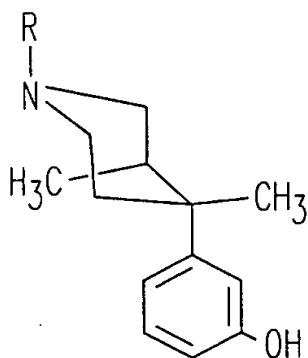
(d) HBr , HOAc ;

FIG. 9A

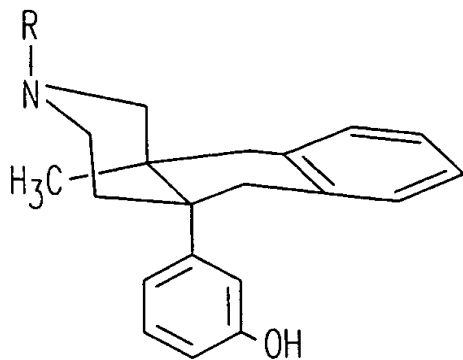
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Naltrexone
(phenylaxial/piperidine chair)

FIG. 9B

3,4-Dimethyl-4-(3-hydroxyphenyl)piperidine
(phenylequatorial/piperidine chair)

FIG. 9C

8a-Methyl-4a-(3-hydroxyphenyl)octahydrobenzo[e]isoquinoline
(phenylequatorial/piperidine chair)

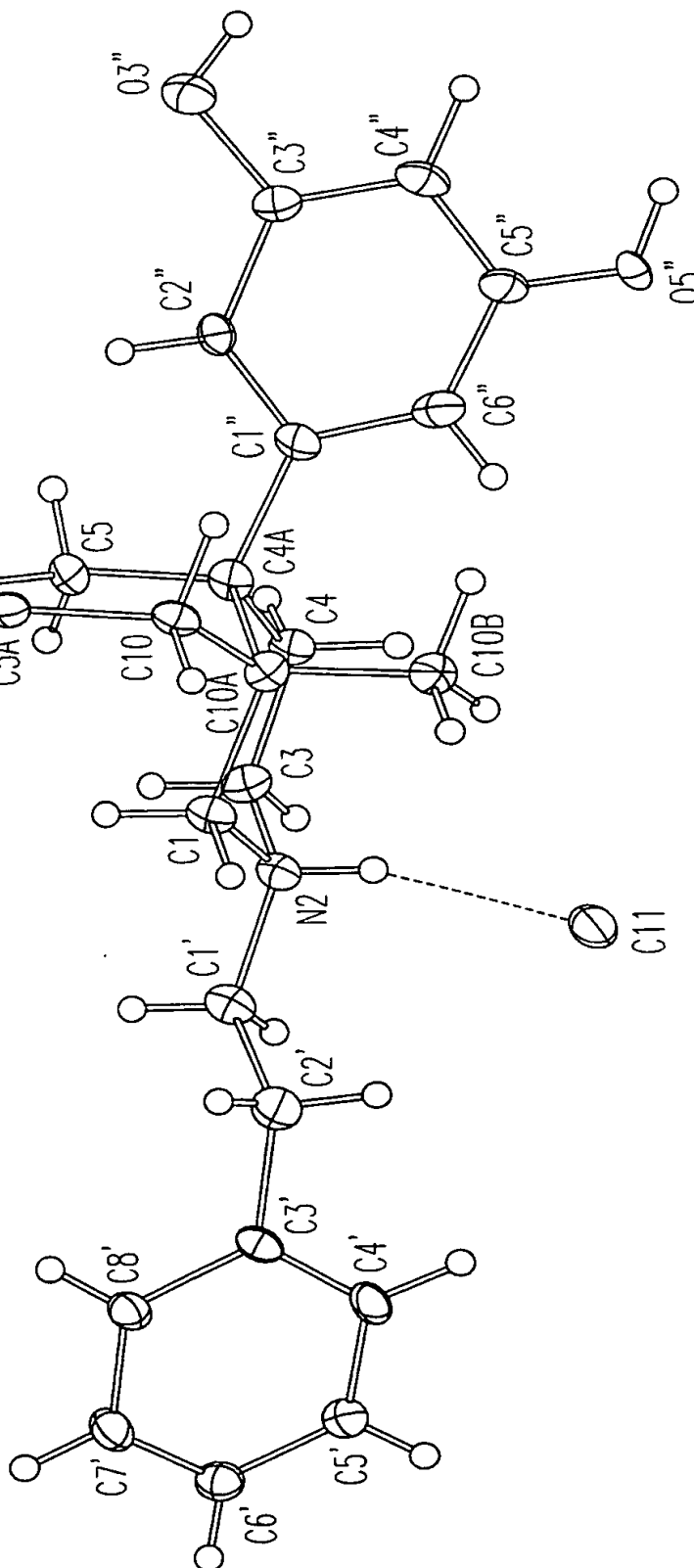
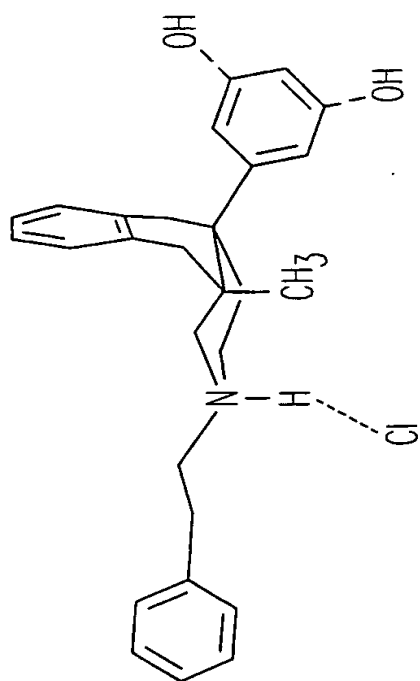
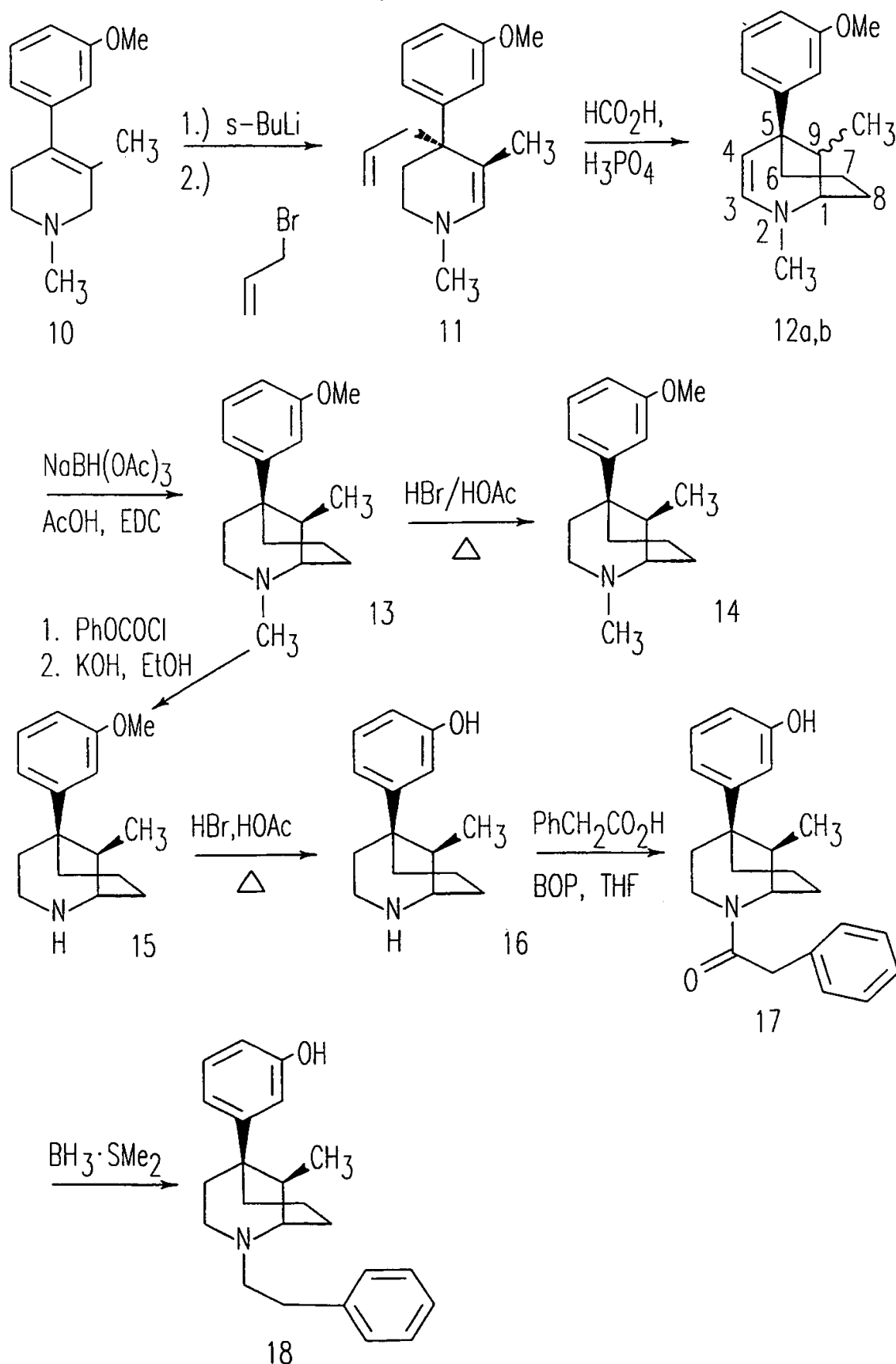


FIG. 10

FIG. 11



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FIG. 12

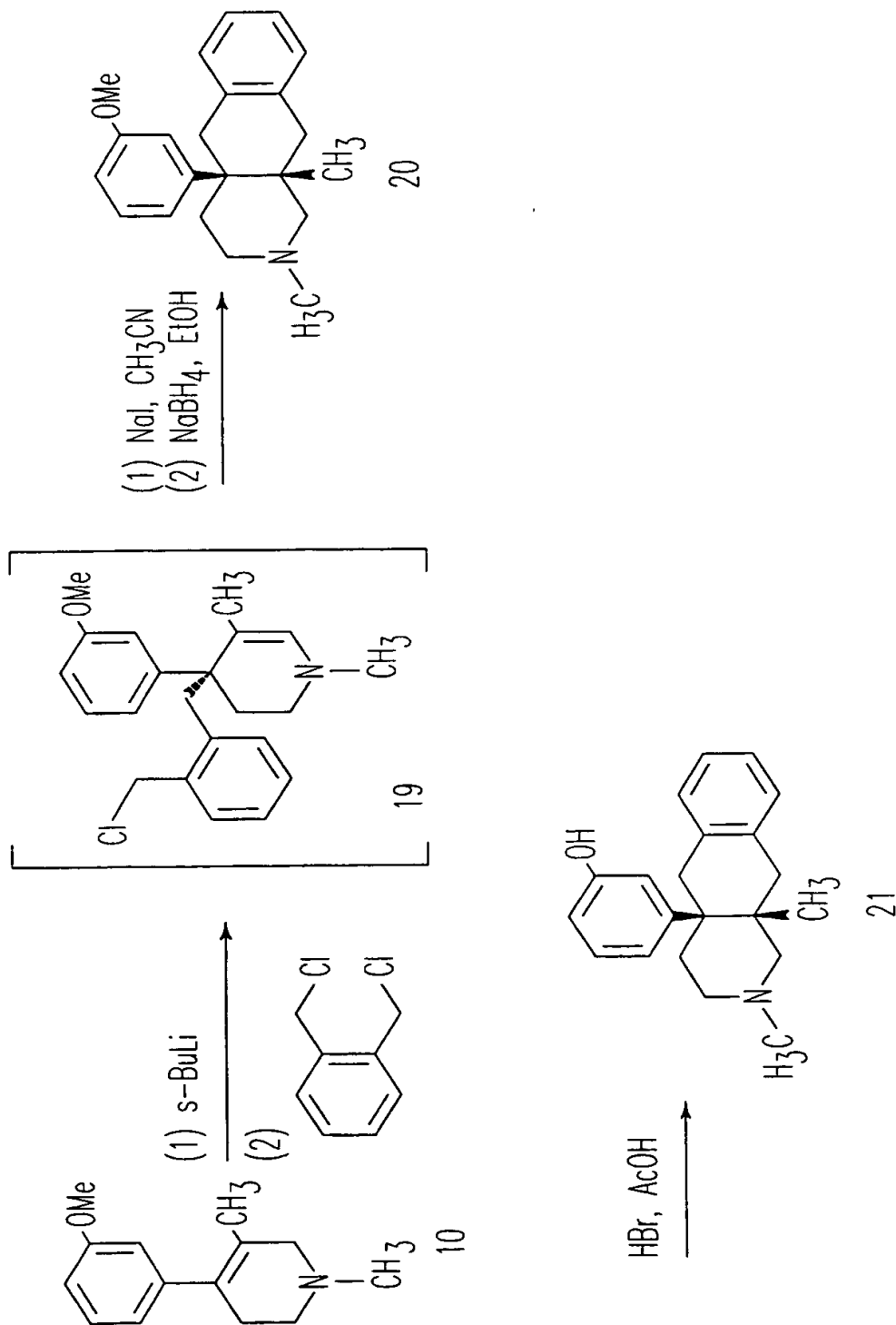
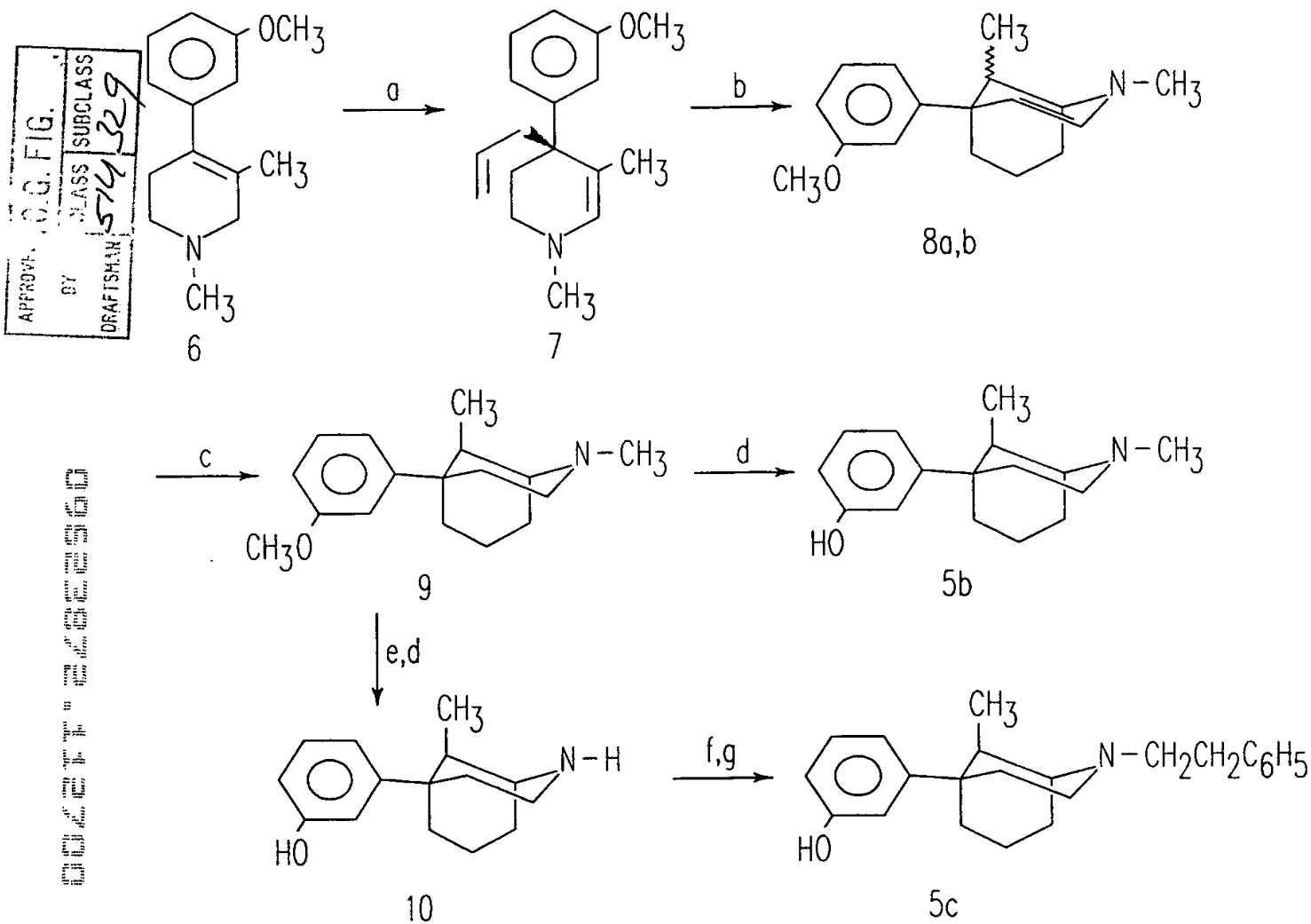


FIG. 13

^a (a) $s\text{-BuLi}$, allyl-Br;(b) H_3PO_4 , HCO_2H ;(c) $\text{NaHB}(\text{OAc})_3$;(d) HOAc , HBr ;(e) PhOCOCI , then KOH , H_2O ;(f) (benzotriazol-1-yloxy)tris(dimethylamino) phosphonium hexafluorophosphate, $\text{PhCH}_2\text{CO}_2\text{H}$;

(g) borane-dimethyl sulfide, THF.

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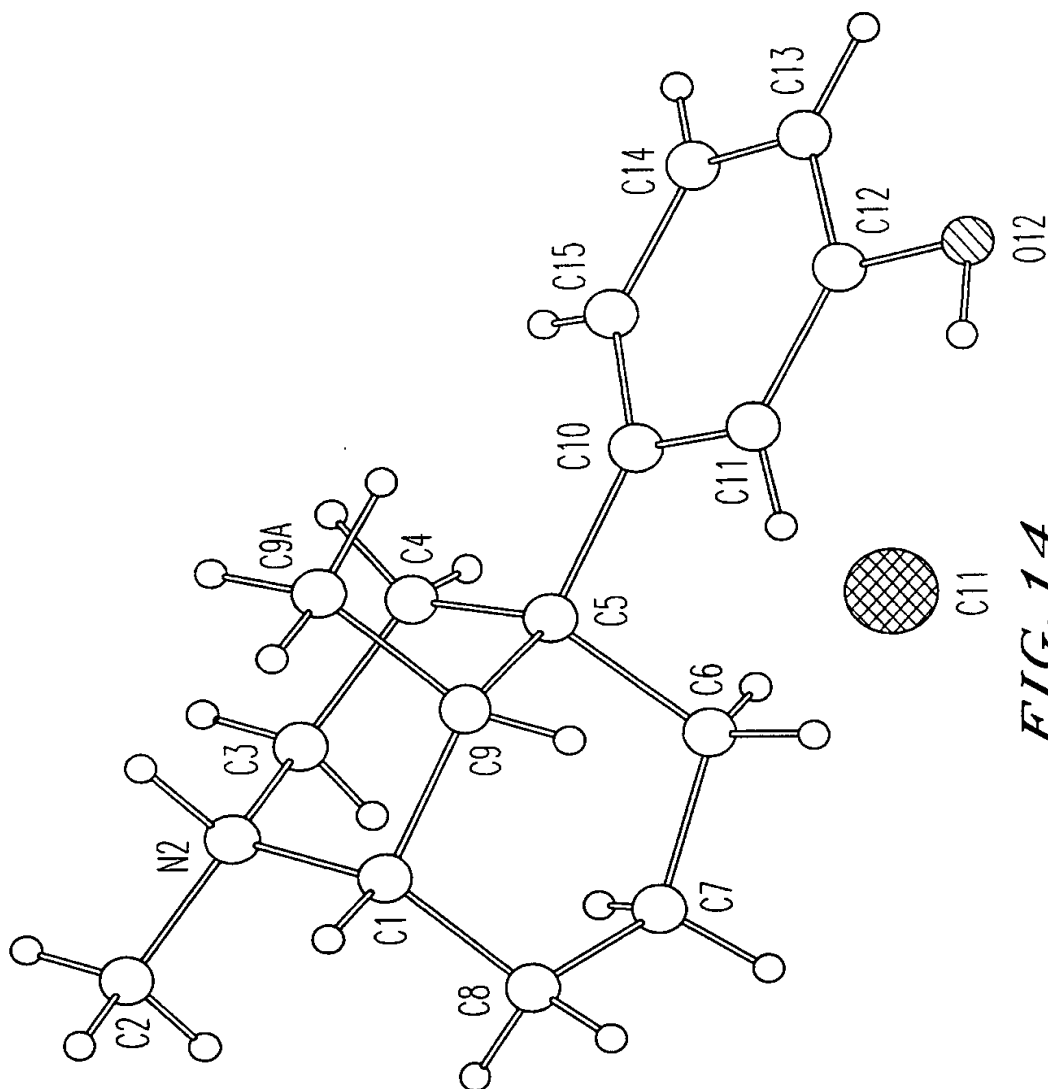
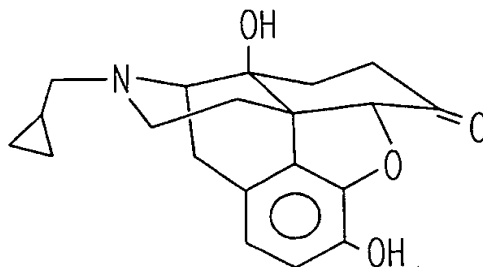


FIG. 14

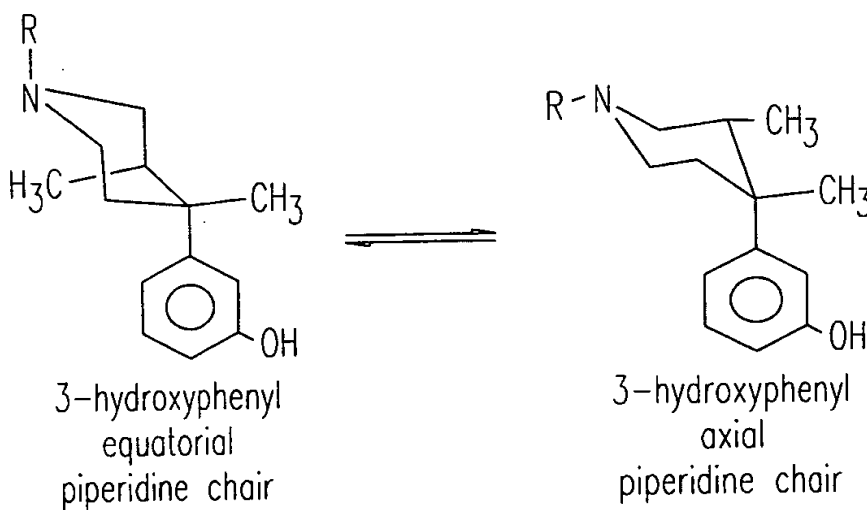
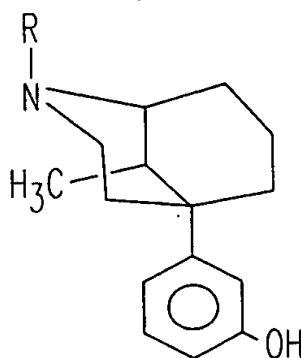
FIG. 15

Naltrexone (1b)



3-hydroxyphenyl axial piperidine chair

3,4-Dimethyl-4-(3-hydroxyphenyl)-piperidine (4)

2-Alkyl-9 β -methyl-5-(3-hydroxyphenyl)-
morphan (5)

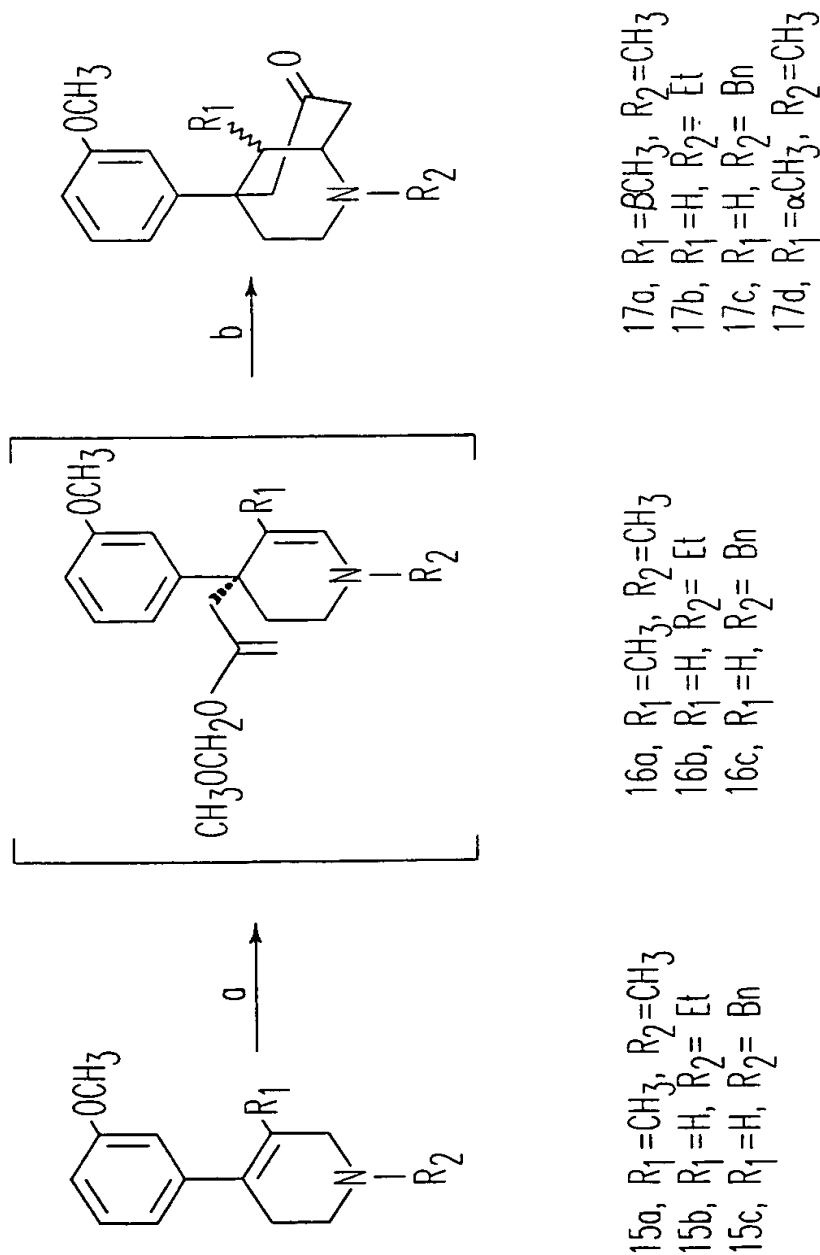
3-hydroxyphenyl equatorial piperidine chair

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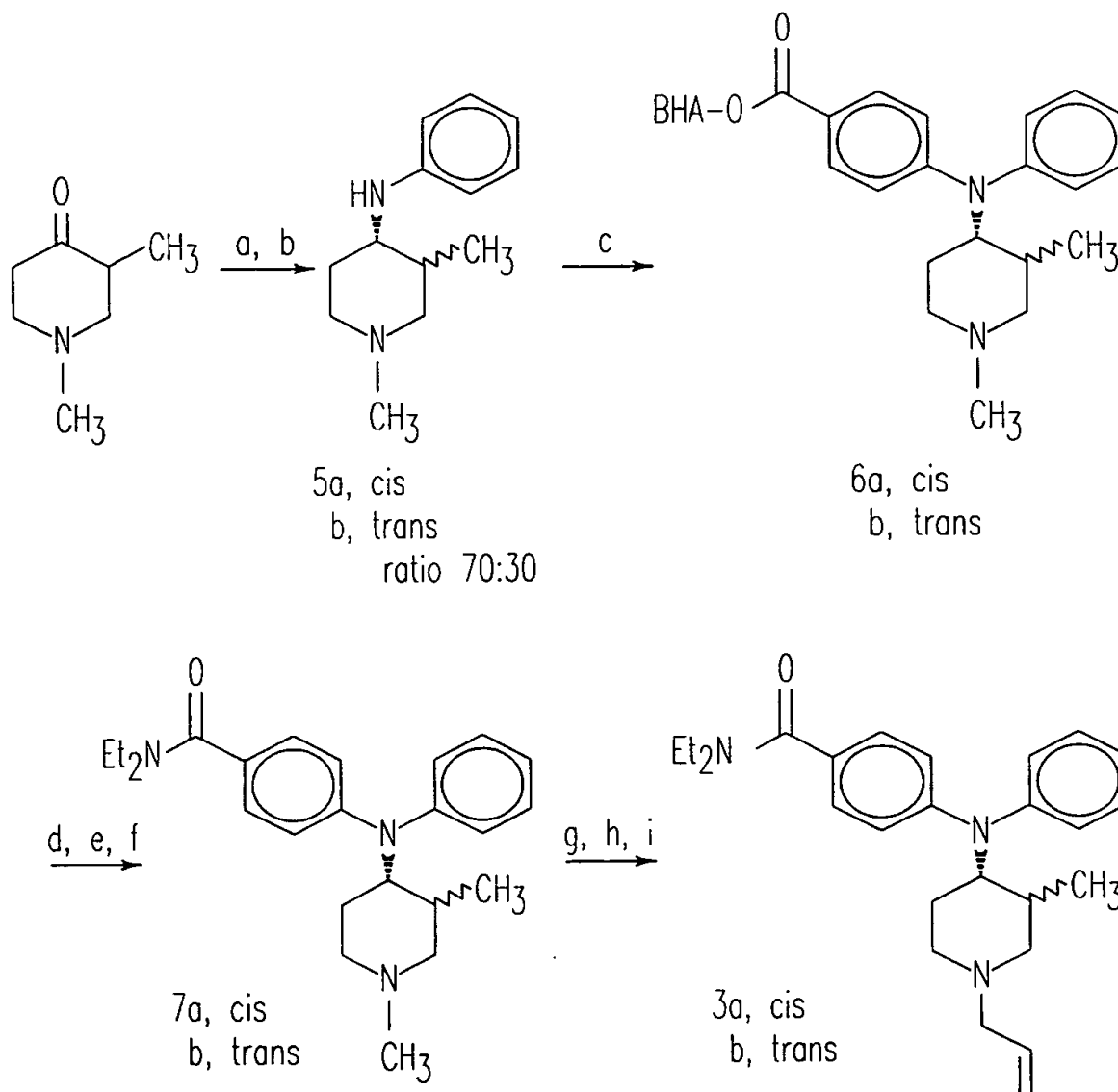
APPROVED	U.R. FIG.	
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FIG. 16



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FIG. 17



Reagents: (a) $\text{Ti}(\text{O}-i\text{-Pr})_4$, aniline; (b) NaBH_4 , EtOH; (c) $n\text{-BuLi}$, THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzonate; (d) N-methylpyrrolidinone, NaOCH_3 , toluene; (e) EtOH, H_2O ; (f) Et_2NH , BOP, Et_3N ; (g) PhOCOCI ; (h) KOH, $i\text{-PrOH}$, H_2O ; (i) allyl-Br, EtOH, K_2CO_3

APPROVED	C.G. FIG.
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FIG. 18

